Published in final edited form as:

Female Pelvic Med Reconstr Surg. 2016 ; 22(1): 24–28. doi:10.1097/SPV.0000000000000215.

Adherence to Oral Therapy for Urgency Urinary Incontinence: Results from the ABC (Anticholinergic vs Botox Comparison) Trial

Anthony G. Visco, M.D.^a, Linda Brubaker, M.D., M.S.^b, J. Eric Jelovsek, M.D., M.M.Ed^c, Tracey S. Wilson, M.D.^d, Peggy Norton, M.D.^e, Halina M. Zyczynski, M.D.^f, Cathie Spino, DSc.^g, Larry Sirls, M.D.^h, John N. Nguyen, M.D.ⁱ, David D. Rahn, M.D.^j, Susan F. Meikle, M.D., M.S.P.H.^k, Tracy L. Nolen, DrPh.^l, and for the Pelvic Floor Disorders Network

^aDepartment of Obstetrics and Gynecology, Duke University Medical Center, Durham, North Carolina, USA

^bDepartments of Obstetrics & Gynecology and Urology, Stritch School of Medicine, Loyola University Chicago, Chicago, Illinois, USA

^cObstetrics, Gynecology & Women's Health Institute, Cleveland Clinic, Cleveland, Ohio, USA

^dDepartment of Urology, University of Alabama at Birmingham, Birmingham, Alabama, USA

^eDepartment of Obstetrics and Gynecology, University of Utah, Salt Lake City, Utah, USA

^fDepartment of Obstetrics, Gynecology and Reproductive Sciences, University of Pittsburgh, Pittsburgh, Pennsylvania, USA

^gDepartment of Biostatistics, University of Michigan, Ann Arbor, Michigan, USA

^hDepartment of Urology, Beaumont Health System, OUWB School of Medicine, Royal Oak, Michigan, USA

ⁱDepartment of Obstetrics and Gynecology, Kaiser Permanente Downey, Downey, California, USA

^jDepartment of Obstetrics and Gynecology, University of Texas Southwestern Medical Center, Dallas, Texas, USA

^kGynecologic Health and Disease Branch, The Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD, USA

^lRTI International, Research Triangle Park, NC USA

Abstract

Corresponding Author: Anthony G. Visco, M.D. Associate Professor and Chief, Division of Urogynecology and Reconstructive Pelvic Surgery, Department of Obstetrics and Gynecology, Duke University Medical Center, 5324 McFarland Drive, Suite 310, Durham, NC 27707, 919-401-1006, Fax: 919-401-1033, anthony.visco@duke.edu.

This trial is registered at www.clinicaltrials.gov under Registration #: NCT01166438.

Medication adherence using pill counts and MEMSCAP® are reasonably correlated.

Objectives—Medication adherence with urgency urinary incontinence (UUI) treatment is challenging and the best assessment methodology is uncertain. We sought to describe adherence with anticholinergic (AC) versus placebo (P) by comparing pill counts and MEMSCAP® event data and to identify factors associated with adherence.

Methods—The randomized controlled Anticholinergic versus Botox Comparison (ABC) trial, of women with moderate-severe idiopathic UUI included 126 participants initiating AC plus placebo bladder injection and 121 receiving placebo pills plus Botox injection. Adherence data on 243 participants (124 AC and 119 P) were calculated by pill count and MEMSCAP® data for each 2-month interval during the 6-month study that allowed for dose escalation/drug change. Overall composite adherence estimates were calculated using the average of both methods and weighted by the duration of each 2-month interval.

Results—Treatment groups had no significant differences in dosing duration ($p=0.76$) or mean adherence (AC: $83.3\% \pm 16.8$ vs. placebo: $84.8\% \pm 13.8$). Only 53% of women met the dichotomous outcome of $>80\%$ adherence during all intervals. Correlation between adherence by pill counts versus MEMSCAP® decreased over time with pill counts demonstrating higher adherence than MEMSCAP® ($r=0.53, 0.50, \text{ and } 0.36$ for each 2-month interval). Lower adherence was associated with higher baseline incontinence severity and better UUI quality of life for the AC group, and with current smoking status in both groups.

Conclusions—Adherence using pill counts and MEMSCAP® were reasonably correlated and similar in both the AC and placebo groups. In the AC group, higher baseline incontinence severity and better UUI QOL were associated with decreased adherence. Smokers were less adherent.

Introduction

Urgency urinary incontinence (UUI) is defined as the “complaint of involuntary loss of urine associated with urgency.”¹ Approximately 5-10 percent of women experience UUI at least monthly with a negative impact on quality of life.² A recent meta-analysis of over 40 randomized controlled trials of anticholinergic medications, the most frequent therapy for overactive bladder and UUI, found reductions ranging from 0.9 to 4.6 incontinence episodes per day.² Although anticholinergics are modestly effective, there is still a gap between observed and potential levels of treatment efficacy. Patient adherence may contribute to this gap.²

Between 20-30% of all medication prescriptions are never filled, this can be as high as 50% for chronic disease medications.^{3,4} For anticholinergic medications, 65-80% of respondents reported discontinuation during a 12-month period.⁵ Reasons for discontinuance included lack of efficacy and unwanted side effects. Little information on oral medication adherence is available for women affected by UUI. Furthermore, the best method to assess adherence in research studies is uncertain.

The Anticholinergic vs Botulinum Comparison (ABC) trial was a randomized trial of women with idiopathic UUI.⁶ Participants received either oral anticholinergic medication plus placebo bladder injection versus oral placebo plus onabotulinumtoxinA (Botox) injection. This planned secondary analysis sought to 1) describe adherence to oral anticholinergic or oral placebo comparing two adherence methods: pill counts and

MEMSCAP®; 2) identify factors associated with adherence; and 3) explore the relationship between adherence and study outcomes. An improved understanding of adherence may allow targeted education and realistic expectations of treatment efficacy and side-effects.⁷

Methods

The ABC trial was a randomized, double-blind, double-placebo-controlled trial designed to compare the effects of intra-detrusor onabotulinumtoxin A injection versus oral anticholinergic therapy to treat women with moderate to severe idiopathic UUI performed at 10 sites of the National Institutes of Health-funded Pelvic Floor Disorders Network. The methods and primary outcome of the ABC trial have been reported previously.^{6,8} Briefly, women with five or more UUI episodes on a 3-day prospective bladder diary were randomized to either receive a 100 unit intradetrusor injection of onabotulinumtoxin A and six months of oral placebo (P), or a placebo saline intradetrusor injection and six months of a standardized regimen of anticholinergic (AC) medication. Subjects in the saline/AC group were started on solifenacin 5 mg daily for the first 2 months. Solifenacin was increased to 10 mg daily at month 2 and subsequently switched to trospium XR 60 mg daily at month 4 if symptoms were not adequately controlled based on a Patient Global Symptom Control (PGSC) score of 1-3.⁶ Participants assigned to the Botox/placebo group were similarly offered dose escalation. All oral study medications were discontinued at 6 months.

Anticholinergic medication or placebo were dispensed in a Medication Event Monitoring Systems (MEMSCAP®) 6 TrackCap system (AARDEX Group, Ltd., Sion, Switzerland) comprised of a MEMSCAP® cap with a unique serial number, and a standard medication bottle labeled with the subject's ID, randomization number and unique bottle ID. The MEMSCAP® system is fitted with a special closure that records the time and date of each opening and closing of the bottle through integrated microcircuitry. At the 2-, 4- and 6-month study visits, MEMSCAP® data from the prior two-month period were uploaded and stored in an encrypted format on centralized, secured servers (medAmigo, AARDEX Group, Ltd., Sion, Switzerland). Additionally, remaining capsules in the bottles were counted and the medication and bottles were returned to the pharmacy at each study visit. Both active and placebo capsules were over-encapsulated and appeared identical, allowing for masked pill counting. No feedback was provided to participants regarding adherence after pill counting was performed.

Adherence estimates were calculated based on both pill counts and MEMSCAP® data. Study-period (0-2 months, 2-4 months, and 4-6 months) as well as overall adherence estimates were calculated as the percent of expected doses taken. Since study medications were prescribed as once-daily medications, the expected dose for each dosing period was defined as length of the dosing interval measured in days. The number of days in each dosing period was calculated by taking the difference between study visits that occurred at injection visit, 2, 4 and 6 months +/- 2 weeks. For example, the expected dose for the 2-4 month period was the number of days between the two and four month visits. To account for the initial dispensation day, one day was added to the overall and 0-2 month expected dose. The number of doses taken based on pill count was calculated as the number of pills dispensed minus the number of pills returned at the following visit. If a bottle was not

returned, pill count adherence for that study period and the overall pill count adherence were not calculated. The number of MEMSCAP® doses was the number of events recorded during the specified study period. A MEMSCAP® dose/event was defined as an opening followed by closure of the MEMSCAP® with at least 3 seconds between opening and closing. Events reported prior to the initial dispense date or after final return of the MEMSCAP® were excluded from adherence calculations. Multiple events on a single day were each counted independently for up to a maximum of three events. Additional events within the 24-hour period were excluded from the calculations. If a MEMSCAP® was not dispensed, was identified as faulty, or was not returned, MEMSCAP® adherence for that study period and the overall MEMSCAP® adherence were not calculated.

A composite adherence was calculated using the following algorithm: 1) If both pill count and MEMSCAP® adherence estimates were available for a study period, then the composite adherence estimate was the average of the two individual estimates; 2) If only one of the two individual adherence estimates was available for a study period, then the composite adherence estimate for that study period was set to the adherence estimate for the available measure; 3) If none of the individual adherence estimates was available for a study period, a composite adherence was not calculated. The overall composite adherence estimate for each subject was calculated as the average adherence across all study periods weighted by the duration of each period. Adherence was capped at 100%.

Statistical analysis was performed using SAS software, version 9.2 (SAS Institute, Cary, NC). To compare adherence measures, Spearman rank correlation coefficients between MEMSCAP® versus pill count data were calculated for each study period. Continuous measures of adherence calculated once per subject were compared between treatment groups using analysis of covariance techniques adjusting for the randomization stratification variables (previous anticholinergic exposure or drug naiveté, baseline UII severity (5-8 vs. 9 UII episodes/3days) and clinical site). Binary variables were compared using Cochran Mantel-Haenszel tests that accounted for randomization strata. Measures calculated by study period and drug dose were compared using a linear mixed model with adherence measure as the outcome, with terms for treatment group, study period (or drug dose/level), and the interaction of treatment group with study period (or drug dose/level) and covariates for each randomization stratification variable. Study participant was treated as a random effect variable to account for the correlation in outcomes over time within a participant. The association between adherence and daily dosing pattern was explored by calculating the Spearman rank correlation coefficient between overall composite adherence and the interquartile range of dosing times.

To identify potential factors associated with adherence, mixed models were used. For each potential predictor of interest, two models were fit for each outcome measure including the fixed effect of treatment group and site. The first model included the covariate only to see whether it is predictive of outcome or a treatment confounder. The second model included the covariate, the treatment by covariate interaction, and the treatment by month by covariate interaction to evaluate whether the prediction differs by treatment arms. Any factors significant at the 0.1 level for either of these models were included in the initial multivariable models, with the final model determined by stepwise variable reduction using

a p-value of 0.1 to retain variables in the model. Baseline age, body mass index (BMI), smoking status, race, ethnicity, education, drug naïve status, incontinence severity, Overactive Bladder Questionnaire Short Form (OABq-SF)^{9,10} score, and medication burden were considered as potential factors associated with adherence. To assess the relationship between adherence and study outcomes, the primary study analyses were repeated for the subset of the study population considered treatment adherent and additional analyses were conducted on the subset treated with actual anticholinergic medication. A participant was considered treatment adherent if she was ≥80% adherent during each study period based on the composite adherence measure. Data were analyzed based on actual treatment received as opposed to randomized treatment. Any outcome data reported after initiation of off-protocol UUI treatments was censored. For continuous endpoints assessed over time, linear mixed models with terms for treatment group, study visit, and the interaction of treatment group with study visit and covariates for each randomization stratification variable were used. For analyses of binary outcome measures assessed over time, similar models were constructed using a robust Poisson regression model assuming Poisson distribution and log link. Aggregate binary measures of efficacy and safety were evaluated using Mantel–Haenszel tests that accounted for randomization strata.

Results

Nearly all (247) of the 249 women randomized to anticholinergic medication (AC) or Botox injection received the intervention (126 received anticholinergic pill with saline injection, and 121 received placebo pills with Botox injection.) Most (241) subjects were available for primary outcome analysis, and there were no significant group differences between treated subjects in any baseline characteristic including age, number of incontinence episodes, or history of any anticholinergic medication (Table 1). By the first post-intervention study visit at one month, both groups demonstrated a significant decrease in daily incontinence episodes that continued through the six-month study period.⁸

Overall Adherence

As determined by the composite measure of pill count and MEMSCAP® data, both groups had similar overall adherence in taking study pills (AC: 83.3% ±16.8 vs. placebo: 84.8% ±13.8, $p=0.45$), without differences by drug/dosing regimen or study period (Table 2). Treatment groups also had similar overall dosing duration (AC: 176.6 ± 30.5 days vs. placebo: 175.8 ± 25.5 days, $p=0.76$), also without significant differences by drug/dosing regimen or study interval. While over 60% of the subjects in both treatment arms were at least 70% adherent within each study period, only 53% of women met the pre-determined dichotomous criterion for “treatment-adherent” (i.e., at least 80% adherent at all three study phases). Correlation between adherence measured by pill counts versus MEMSCAP® decreased over the treatment period ($r=0.53, 0.50$, and 0.36 for each 2-month interval) with adherence estimates obtained via pill counts tending to be higher than estimates obtained via MEMSCAP® and with a slight waning in adherence (by all measures) over 6 months (Figures 1 and 2). Subjects with more variability in their dosing schedule time tended to be less adherent ($r=0.47, p<0.0001$). Figures 3 and 4 are limited to participants receiving active

therapy. Figure 3 shows the adherence across the various dosages and Figure 4 shows adherence based on whether the subject received dose escalation/drug change.

Factors Associated with Adherence

Using adherence as a continuous measure, factors significantly associated with lower adherence included higher (worse) incontinence severity at baseline (i.e. more frequent episodes of UUI), higher (better) baseline OAB quality of life scores for the AC group, and current smoking status overall (Table 3). Examination of the parameter estimates shows that for every additional urgency incontinence episodes per day, compliance decreases by 1.7%. While these findings are statistically significant they may not represent a significant enough change to be clinically relevant. Similarly, the statistical relationship observed between OAB QOL scores and adherence was not clinically meaningful. When “treatment-adherent” (defined by at least 80% adherence using the composite measure from pill counts and MEMSCAP® data) is used as a dichotomous variable, age, race, and baseline incontinence severity were factors appearing significant ($p < 0.1$) in univariate modeling, only race remained significant in the final multivariable model. In this patient cohort, white race was 76.9% treatment-adherent whereas black or other races were 53.9% and 51.6% treatment-adherent, respectively.

Relationship between Adherence and Study Outcomes

Similar to the findings of the primary intention to treat analyses, there was no significant difference between treatment groups in the reduction of the frequency of episodes of urgency incontinence or improvements in quality of life within the subgroup of treatment-adherent women. In order to explore whether strict treatment adherence was temporally associated with treatment effect, we performed a subanalysis restricted to the subgroup of women randomized to receive active anticholinergic medication. For this analysis we compared participants who were adherent (i.e., those taking pills 5 or more days out of 7 as assessed solely by MEMSCAP® in the week prior to scheduled outcome assessment), versus those who were not.

The observed trend overall showed slightly more improvement for most of the outcomes measured, including >75% reduction from baseline in mean UUI episodes per day by diary, no UUI, and total scores from the PFDI and PFIQ. However, none were statistically or clinically significant. At particular time points (4 and 6 months for reduction from baseline mean UUI episodes, and 4 months for no UUI), these trends were not observed. A sensitivity analysis showed similar improvements in most, but not all, outcome measures when we excluded subjects with large discrepancies in adherence between pills counts and MEMSCAP® (i.e. >30% discrepancy). Overall, adherence based on MEMSCAP® data was not associated with improved continence.

Discussion

Medication adherence is considered important, especially for chronic conditions, but is poorly understood. In clinical care, prescribers hope for 100% adherence with oral medication, yet are well aware of the reality of suboptimal adherence. Increased health care

costs, health care utilization and susceptibility to adverse drug reactions result from suboptimal treatment.¹¹ In OAB patients, Balkrishnan found that every 10% increase in medication possession ratios (MPR) resulted in a 5.6% reduction in annual health care costs.¹² Effective interventions require attention to the multiple conditions and behaviors that influence decisions regarding adherence.¹³

We did not find a statistically significant relationship between adherence and the study outcomes. As this was a secondary analysis, it is possible that we were underpowered for this comparison. However, the differences observed were not clinically relevant. In this study, we confirmed that strict adherence with oral medications for urinary incontinence is low; only 53% of our subjects consistently maintained at least 80% adherence during each phase during the initial 6 months. Yeaw et al. found that 12-month adherence rates were lowest in patients on overactive bladder medications compared to other chronic therapies such as statins, oral anti-diabetics and angiotensin II receptor blockers (35% vs. 61%, 72% and 66%, respectively).¹¹ Adherence in this study is likely higher than that of routine clinical care, given the highly structured environment of a randomized trial, and careful attention to management of side effects (e.g., recommendations to use candy, lozenges, gum or mouthwash to combat dry mouth side effects and to modestly increase fluid intake).^{6,14} D'Souza et al. found adherence rates (measured by the percentage of patients with MPR > 80% for one year) of only 30% in a retrospective cohort study of OAB pharmacy claims data.¹⁵ Using data from a national prescription database, Norwegian investigators have also documented high discontinuation rates for OAB medications and a low proportion (60%) of adherence during treatment.¹⁶

This study documents the importance of measuring medication adherence when measuring treatment efficacy as one should not assume that all prescribed medications are taken as directed. Similar to Liu et al., we found that adherence may be underestimated using MEMSCAP® and overestimated by using pill counts alone.¹⁷ We combined both measures of adherence in an attempt to provide a more accurate composite measurement of adherence. The correlation of adherence calculations using pill counts and MEMSCAP® should inform future trial design and help advance our understanding of research methods for measurement of adherence. Our findings that adherence declines over time and subjects who were less consistent in their daily dosing schedule were less adherent overall are consistent with clinical experience.

It is likely that the relationship between smoking and decreased adherence is secondary to a general pattern of poor health behaviors. Others have found that higher levels of general health are associated with better adherence in multivariable analyses of medical claims studies.^{15,18} However, we found it somewhat paradoxical that women with worse incontinence were less adherent, yet women with better quality of life scores were also suboptimally adherent. This intriguing finding deserves further study and may be explained by differences in treatment expectations.

This study provides robust adherence information for oral UUI medication outside an industry-sponsored setting. Research strengths include multiple clinical sites, diversity of participants and two methods of adherence assessment. Nonetheless, we noted multiple

challenges in our attempts to measure adherence, including pill count patterns that may indicate that subjects did not follow study protocols. It is not uncommon for clinical patients to remove medication from a prescription bottle in order to fill a secondary “day-by-day” dispenser. Although we cannot confirm this behavior, this occurrence would have potentially decreased the accuracy of the MEMSCAP® recordings. Finally, we cannot comment on adherence beyond the duration of our adherence follow-up measures at 6 months.

In conclusion, we believe that our finding show that adherence based on pill counts and MEMSCAP® were reasonably correlated and similar in both the active and placebo groups for participants receiving oral UUI medication. Future studies are encouraged to further refine research measures of medication adherence as well as clinically useful methods to optimize adherence during standard clinical care.

Acknowledgments

Supported by grants from The *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, (Duke: 2-U10-HD04267-12, Loyola:U10-HD054136, UAB: 2-U10-HD041261-11, Utah: U10-HD041250, Cleveland Clinic: 2-U10-HD054215-06, UCSD: 2-U10-HD054214-06, Pittsburgh: 1-U10-HD069006-01, UTSW: 2-U10-HD054241-06, Univ. of Michigan: U01-HD41249, RTI: 1-U01-HD069010-01) and the NIH Office of Research on Women's Health

References

1. Haylen BT, de Ridder D, Freeman RM, et al. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for female pelvic floor dysfunction. *Neurourology and urodynamics*. 2010; 29:4–20. [PubMed: 19941278]
2. Hartmann KE, McPheeters ML, Biller DH, et al. Treatment of overactive bladder in women. Evidence report/technology assessment. 2009:1–120. [PubMed: 19947666]
3. Haynes RB, Ackloo E, Sahota N, McDonald HP, Yao X. Interventions for enhancing medication adherence. *Cochrane Database Syst Rev*. 2008:CD000011. [PubMed: 18425859]
4. Peterson AM, Takiya L, Finley R. Meta-analysis of trials of interventions to improve medication adherence. *American journal of health-system pharmacy : AJHP : official journal of the American Society of Health-System Pharmacists*. 2003; 60:657–65. [PubMed: 12701547]
5. Wagg A, Compion G, Fahey A, Siddiqui E. Persistence with prescribed antimuscarinic therapy for overactive bladder: a UK experience. *BJU international*. 2012; 110:1767–74. [PubMed: 22409769]
6. Visco AG, Brubaker L, Richter HE, et al. Anticholinergic versus botulinum toxin A comparison trial for the treatment of bothersome urge urinary incontinence: ABC trial. *Contemporary clinical trials*. 2012; 33:184–96. [PubMed: 22008247]
7. Benner JS, Nichol MB, Rovner ES, et al. Patient-reported reasons for discontinuing overactive bladder medication. *BJU international*. 2010; 105:1276–82. [PubMed: 19912188]
8. Visco AG, Brubaker L, Richter HE, et al. Anticholinergic therapy vs. onabotulinumtoxin A for urgency urinary incontinence. *The New England Journal of Medicine*. 2012; 367:1803–13. [PubMed: 23036134]
9. Coyne KS, Matza LS, Thompson C, Jumadilova Z, Bavendam T. The responsiveness of the OAB-q among OAB patient subgroups. *Neurourology and urodynamics*. 2007; 26:196–203. [PubMed: 17016794]
10. Matza LS, Thompson CL, Krasnow J, Brewster-Jordan J, Zyczynski T, Coyne KS. Test-retest reliability of four questionnaires for patients with overactive bladder: The overactive bladder questionnaire (OAB-q), patient perception of bladder condition (PPBC), urgency questionnaire (UQ), and the primary OAB symptom questionnaire (POSQ). *Neurourology and urodynamics*. 2005; 24:215–25. [PubMed: 15747340]

11. Yeaw J, Benner JS, Walt JG, Sian S, Smith DB. Comparing adherence and persistence across 6 chronic medication classes. *Journal of managed care pharmacy : JMCP*. 2009; 15:728–40. [PubMed: 19954264]
12. Balkrishnan R, Bhosle MJ, Camacho FT, Anderson RT. Predictors of medication adherence and associated health care costs in an older population with overactive bladder syndrome: a longitudinal cohort study. *The Journal of urology*. 2006; 175:1067–71. discussion 71-2. [PubMed: 16469620]
13. Steiner JF. Rethinking adherence. *Annals of internal medicine*. 2012; 157:580–5. [PubMed: 23070491]
14. Staskin DR, MacDiarmid SA. Using anticholinergics to treat overactive bladder: the issue of treatment tolerability. *The American journal of medicine*. 2006; 119:9–15. [PubMed: 16483863]
15. D'Souza AO, Smith MJ, Miller LA, Kavookjian J. An appraisal of pharmacoeconomic evidence of maintenance therapy for COPD. *Chest*. 2006; 129:1693–708. [PubMed: 16778291]
16. Mauseth SA, Skurtveit S, Spigset O. Adherence, persistence and switch rates for anticholinergic drugs used for overactive bladder in women: data from the Norwegian Prescription Database. *Acta obstetricia et gynecologica Scandinavica*. 2013
17. Liu H, Golin CE, Miller LG, et al. A comparison study of multiple measures of adherence to HIV protease inhibitors. *Annals of internal medicine*. 2001; 134:968–77. [PubMed: 11352698]
18. Staskin D, Sand P, Zinner N, Dmochowski R, Trosipium Study G. Once daily trospium chloride is effective and well tolerated for the treatment of overactive bladder: results from a multicenter phase III trial. *The Journal of urology*. 2007; 178:978–83. discussion 83-4. [PubMed: 17632131]

Figure 1. Mean (+/-SD) % Adherence for Anticholinergics/Placebo By Study Period

Figure 2. Mean (+/-SD) % Adherence for Anticholinergics/Placebo By Drug/Dose Level

Figure 3. Mean (+/-SD) % Adherence in the Anticholinergics Group Only By Drug/Dose Level

Figure 4. Mean (+/-SD) % Adherence in the Anticholinergics Group Only By Dose Escalation Group

Table 1
Baseline Characteristics of Randomized Groups

	Anticholinergic N=126	Botox N=121
Age, years	56.7 ($\pm$ 11.6)	59.3 ($\pm$ 10.8)
Hispanic	22 (17%)	22 (18%)
Race:		
White	98 (78%)	96 (79%)
Black	23 (18%)	18 (15%)
Other	5 (4%)	7 (6%)
BMI, kg/m ²	32.9 ($\pm$ 8.2)	32.1 ($\pm$ 7.0)
Smoking (current)	12 (10%)	15 (12%)
Premenopausal	22 (17%)	15 (12%)
Baseline PVR, mL	35.4 ($\pm$ 47.4)	36.6 ($\pm$ 44.6)
No prior anticholinergics - Drug naïve	54 (43%)	48 (40%)
UUI episodes per day	5.2 ($\pm$ 2.7)	4.8 ($\pm$ 2.7)

Data presented as mean ($\pm$ SD) or n (%)

BMI=body mass index, PVR=post-void residual, UUI=urgency urinary incontinence

Table 2
Adherence rates by treatment group

Study Period or Dosing Regimen		Anticholinergic (N=124)	Botox (Placebo pills) (N=119)	P-value
Duration of dosing, <i>days</i>				
	0-2 Months	60.4 (10.5)	61.4 (10.3)	0.54
	2-4 Months	59.9 (10.4)	57.9 (10.2)	
	4-6 Months	56.7 (15.0)	56.6 (13.2)	
	Overall	176.6 (30.5)	175.8 (25.5)	0.76
Adherence (composite measure), <i>percent</i>				
By Dosage	Solifenacin 5 mg	83.8 (19.0)	84.9 (16.3)	0.16
	Solifenacin 10 mg	78.2 (24.8)	81.6 (21.2)	
	Trospium XR 60 mg	76.1 (26.5)	81.0 (17.5)	
By Time Period				
	0-2 Months	85.5 (18.5)	87.0 (16.7)	0.30
	2-4 Months	82.2 (22.5)	85.5 (16.1)	
	4-6 Months	80.6 (19.5)	80.7 (19.2)	
	Overall	83.3 (16.8)	84.8 (13.8)	0.45
Subjects Adherent By Various Definitions of Treatment Adherence (composite measure):				
	At 80% Adherence, n (%)	66 (53%)	63 (53%)	0.82
	At 70% Adherence, n (%)	74 (60%)	78 (66%)	0.55
	At 60% Adherence, n (%)	89 (72%)	83 (70%)	0.76

Data presented as mean days or percent (SD) except where otherwise noted

Table 3
Final Predictors of % Anticholinergic/Placebo Adherence (composite measure)

<i>Characteristic</i>	<i>Estimate (SE)</i>
Adjusted Mean Estimates of % Adherence for Categorical Predictors	
Overall Treatment Group	
Anticholinergic	81.4 (1.8)
Botox	83.3 (1.9)
Smoking Status	
Never	85.6 (1.7)
Previous	84.5 (1.9)
Current	76.8 (3.3)
Month by Treatment Group	
Anticholinergic – 0-2 Months	84.5 (2.0)
Anticholinergic – 2-4 Months	80.9 (2.0)
Anticholinergic – 4-6 Months	78.7 (2.0)
Botox – 0-2 Months	86.1 (2.1)
Botox – 2-4 Months	84.5 (2.1)
Botox – 4-6 Months	79.1 (2.1)
Parameter Estimates for Continuous Predictors (effect of 1 unit change on % Adherence)	
Baseline Mean UUIE/day by Treatment Group	
Anticholinergic	-1.7 (0.59)
Botox	0.43 (0.62)
Baseline OAB QOL Score by Treatment Group	
Anticholinergic	-0.17 (0.07)
Botox	0.12 (0.08)

NOTE: The model was adjusted for clinical site.